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Registration Decision RD2015-18

BLAD polypeptide

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Registration Decision for BLAD polypeptide

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is granting full registration for the sale and use of Problad Technical Fungicide and Fracture Fungicide (previously known as Problad Plus), containing the technical grade active ingredient BLAD polypeptide, to be used to suppress or control powdery mildew and grey mould on grape, strawberry, tomato, stone fruit, almond and ornamental plants.

An evaluation of available scientific information found that, under the approved conditions of use, the product has value and does not present an unacceptable risk to human health or the environment.

These products were first proposed for registration in the consultation document[1] Proposed Registration Decision PRD2015-01, *BLAD polypeptide*. This Registration Decision[2] describes this stage of the PMRA's regulatory process for BLAD polypeptide and summarizes the Agency's decision, the reasons for it and provides, in Appendix I, a summary of comments received during the consultation process as well as the PMRA's response to these comments. This decision is consistent with the proposed registration decision stated in PRD2015-01.

For more details on the information presented in this Registration Decision, please refer to the Proposed Registration Decision PRD2015-01, *BLAD polypeptide* that contains a detailed evaluation of the information submitted in support of this registration.

What Does Health Canada Consider When Making a Registration Decision?

The key objective of the *Pest Control Products Act* is to prevent unacceptable risks to people and the environment from the use of pest control products. Health or environmental risk is considered acceptable[3] if there is reasonable certainty that no harm to human health, future generations or the environment will result from use or exposure to the product under its conditions of registration. The Act also requires that products have value[4] when used according to label directions. Conditions of registration may include special precautionary measures on the product label to further reduce risk.

To reach its decisions, the PMRA applies modern, rigorous risk-assessment methods and policies. These methods consider the unique characteristics of sensitive subpopulations in humans (for example, children) as well as organisms in the environment. These methods and policies also consider the nature of the effects observed and the uncertainties when predicting the

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1 "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*.

2 "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act*.

3 "Acceptable risks" as defined by subsection 2(2) of *Pest Control Products Act*.

4 "Value" as defined by subsection 2(1) of *Pest Control Products Act* "... the product's actual or potential contribution to pest management, taking into account its conditions or proposed conditions of registration, and includes the product's (*a*) efficacy; (*b*) effect on host organisms in connection with which it is intended to be used; and (*c*) health, safety and environmental benefits and social and economic impact".

impact of pesticides. For more information on how the PMRA regulates pesticides, the assessment process and risk-reduction programs, please visit the Pesticides and Pest Management portion of Health Canada's website at healthcanada.gc.ca/pmra.

What Is BLAD polypeptide?

BLAD polypeptide is a fragment of a naturally occurring seed storage protein in sweet lupine (*Lupinus albus*) that serves as a nitrogen source for the germinating and developing plant. It also acts on susceptible fungal pathogens by causing damage to the fungal cell wall and disrupting the inner cell membrane. BLAD polypeptide is not yet classified by the Fungicide Resistance Action Committee, but based on the proposed mode of action, the risk of resistance is considered to be small.

Health Considerations

Can Approved Uses of BLAD polypeptide Affect Human Health?

BLAD polypeptide is unlikely to affect human health when it is used according to label directions.

Potential exposure to BLAD polypeptide may occur when handling and applying the end-use product, Fracture Fungicide. When assessing health risks, two key factors are considered: the levels where no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (for example, children and nursing mothers). Only uses for which the exposure is well below levels that cause no effects in animal testing are considered acceptable for registration.

In laboratory animals, the acute toxicity of the end-use product, Fracture Fungicide, containing BLAD polypeptide, was low via the oral, dermal, and inhalation routes of exposure. Fracture Fungicide is mildly irritating to the skin and eyes; consequently, the hazard signal words "CAUTION; EYE AND SKIN IRRITANT" are required on the Fracture Fungicide label. Fracture Fungicide is not a dermal sensitizer.

A request to bridge acute toxicity data from the end-use product to the technical grade active ingredient was considered to be acceptable. The active ingredient, BLAD polypeptide, was considered to be of low acute toxicity via the oral, dermal, and inhalation routes of exposure. BLAD polypeptide was mildly irritating to the skin and eyes; consequently, the hazard signal words "CAUTION; EYE AND SKIN IRRITANT" are required on the Problad Technical Fungicide label. BLAD polypeptide is not a dermal sensitizer.

BLAD polypeptide is not expected to cause effects in developing young or to cause damage to genetic material when used according to the label instructions.

BLAD polypeptide is not expected to elicit an allergic response in individuals who are sensitive to allergens present in lupine seeds and/or other legumes. In addition, all products manufactured for import into Canada will be required to ensure the absence of primary allergen components (i.e. levels are below the level of detection).

The risk assessment protects against the effects of BLAD polypeptide by ensuring that the level of human exposure is well below the lowest dose at which effects occurred in animal tests.

Risks in Residential and Other Non-Occupational Environments

Estimated risk for non-occupational exposure is not of concern provided that directions specified on the label are observed.

Residential exposure to individuals coming in contact with Fracture Fungicide from drift during application is not expected to result in unacceptable risk when Fracture Fungicide is used according to label directions.

Occupational Risks From Handling and Applying Fracture Fungicide

Occupational risks are not of concern when Fracture Fungicide is used according to the label directions, which include protective measures.

An assessment conducted for individuals handling and applying Fracture Fungicide indicated that the risk is not of concern when the product is used according to label directions.

Residues in Water and Food

Dietary risks from food and drinking water are not of health concern.

Dietary risks from food and drinking water are expected to be negligible given the low toxicity, the lack of quantifiable residues from the supplemental residue information, and the likelihood (most likely negligible) that exposure of individuals with lupine and/or other legume (for example, peanut) sensitivities to Fracture Fungicide will result in an allergic reaction. Consequently, the specification of a maximum residue limit (MRL) under the *Pest Control Products Act* is not being recommended.

Environmental Considerations

What Happens When BLAD Polypeptide Is Introduced Into the Environment?

Problad Technical Fungicide will enter the environment when applied as Fracture Fungicide to grapes, strawberries, tomatoes, stone fruit, and ornamentals. Problad Technical Fungicide will dissipate in the environment primarily through microbial degradation. The risk to non-target aquatic and terrestrial organisms in the environment is negligible.

BLAD Polypeptide is a naturally-occurring seed storage protein, which accumulates exclusively in the cotyledons of Lupinus species (for example, *Lupinus albus*), between days four and twelve after the onset of germination. It is a 20kDa polypeptide of β-conglutin, or characterized as a fragment of the amino acid sequence of β-conglutin. Th β-conglutin protein is classified as a 7S globulin which is part of the broader family of cupin proteins, which provides a major nitrogen source for germination of the developing plant.

Fracture Fungicide is a non-systemic biofungicide with strong antifungal activities both preventive but also for control. The non-toxic mode of action is described as binding very strongly to chitin in fungal cell walls, inhibiting any fungal growth. The active ingredient degrades chitin by catalyzing the successive removal of the *N*-acetyl-D-glucosamine terminal chitin monomers, and destroying the fungal cells.

BLAD Polypeptide is readily biodegradable and non-toxic to all non-target organisms tested, both terrestrial and aquatic. Therefore, the risk to non-target aquatic and terrestrial organisms in the environment is negligible when Fracture Fungicide is used according to the label directions.

Value Considerations

What Is the Value of Fracture Fungicide?

Fracture Fungicide is a broad spectrum biological fungicide with a unique mode of action that will contribute to resistance management when integrated with cultural methods and chemical sprays in an Integrated Pest Management (IPM) program.

Fracture Fungicide provides non-systemic, preventative action when applied to plant foliage with activity against powdery mildew and grey mould on fruit, vegetable and ornamental crops and blossom blight on stone fruit.

Measures to Minimize Risk

Registered pesticide product labels include specific instructions for use. Directions include risk-reduction measures to protect human and environmental health. These directions must be followed by law.

The key risk-reduction measures on the label of Fracture Fungicide to address the potential risks identified in this assessment are as follows:

Key Risk-Reduction Measures

Human Health

Both Problad Technical Fungicide and Fracture Fungicide labels must include the statement, "CAUTION – SKIN AND EYE IRRITANT" on the principal display panel and "May irritate skin and eyes" and "Avoid contact with the skin and eyes" on the secondary display panel.

To avoid direct contact with Fracture Fungicide on the skin and eyes, workers involved in the mixing, loading, application, cleaning, and maintenance of machinery must wear long-sleeved shirts, long pants, chemical-resistant gloves, shoes, socks, and protective eyewear.

To avoid inadvertent bystander exposure during application, the Fracture Fungicide label must include the statement, "Apply only when the potential for drift to areas of human habitation or areas of human activity such as houses, cottages, schools, and recreational areas is minimal. Take into consideration wind speed, wind direction, temperature, application equipment, and sprayer settings."

Other Information

The relevant test data on which the decision is based (as referenced in PRD2015-01, *BLAD polypeptide)* are available for public inspection, upon application, in the PMRA's Reading Room (located in Ottawa). For more information, please contact the PMRA's Pest Management Information Service by phone (1-800-267-6315) or by e-mail (pmra.infoserv@hc-sc.gc.ca).

Any person may file a notice of objection[5] regarding this registration decision within 60 days from the date of publication of this Registration Decision. For more information regarding the basis for objecting (which must be based on scientific grounds), please refer to the Pesticides and Pest Management portion of the Health Canada's website (Request a Reconsideration of Decision) or contact the PMRA's Pest Management Information Service.

[5] As per subsection 35(1) of the *Pest Control Products Act.*

Appendix I Comments and Responses

The following comment was received during the consultation period:

"The consultation document state that the active ingredient "binds very strongly to chitin" and "The active ingredient degrades chitin by catalyzing the successive removal of the N-acetyl-D-glucosamine terminal chitin monomers...". Given the above statements, it seems very plausible that the active ingredient would have harmful effects on the growth of insect larvae over time (i.e. over a periods of days), moulting, etc. and chitin inhibition is a known avenue of insect control.

- was the active ingredient tested on insect larvae growth or moulting?
- if it was tested, how, and with what species?
- Can the results of these tests be provided to individuals.

PMRA Response

A laboratory study, following accepted guidelines, Good Laboratory Practices and conducted with the aphid parasitoid wasp, *Aphidius rhopalosiphi*, was submitted and showed no adverse effects on mortality or reproduction of *A. rhopalosiphi* up to an equivalent of 17.073 g BLAD Polypeptide/ha. This is almost three times the highest single application rate of Fracture Fungicide (up to 3.3 L/ha at 20% concentration = 6.6 g Fracture Fungicide /ha). The results of acute oral and contact studies with honeybees showed no toxicity to these insects by these routes of exposure. Also, Fracture Fungicide is not a systemic fungicide, is not expected to be translocated through treated plants to pollen and nectar, and is not expected to persist in the environment (due to rapid biotransformation). Therefore, although insect growth and moulting were not tested directly, based on the information presented here, Fracture Fungicide is not expected to cause adverse effects to non-target organisms in the environment. A similar conclusion was supported and published by the USEPA.

The relevant test data on which the decision is based (as referenced in PRD2015-01, *BLAD polypeptide)* are available for public inspection, upon application, in the PMRA's Reading Room (located in Ottawa). For more information, please contact the PMRA's Pest Management Information Service by phone (1-800-267-6315) or by e-mail (pmra.infoserv@hc-sc.gc.ca).